pentone, 2-3 ml., is given to produce unconsciousness, and tracheal intubations may then be performed with ease.

The patient is transferred to the theatre, where small doses of relaxants are given when required. Oxygen is administered if the respiratory excursion is inadequate, particularly in those cases requiring the steep Trendelenburg position. In prolonged operations, if the pulse rate begins to rise we have been able to re-establish control by a small supplementary dose of the original mixture. Great care is taken to replace any blood lost, as the patient is not able to compensate for gross diminution or increase of circulation blood volume. Our experience so far has been of patients aged from 28 to 76 years, and has included the following operations: gastrectomies, Wertheim's hysterectomies, hysterectomies, total colectomies, anterior pelvic exenterations, adherent malignant ovarian cysts, laminectomies, bilateral mastectomy and a second operation of prostatectomy on the same patient, together with less extensive operations in patients who would normally be considered poor risks.

#### Case Reports

Case 6.—A married woman aged 76, weighing 8 st. 4 lb. (52.6 kg.), had had two operations for carcinoma of the body of the uterus. She was admitted for symptoms of largebowel obstruction with a large tumour arising from the pelvis with ascites. B.P. was 180/120. Six hours after admission she developed gross cardiac irregularity and electrocardiography indicated a coronary infarction. She was thought to be unfit for operative intervention. Two days later her condition became grave and fibrillation was occurring at a rate of 140, with a pulse deficit of 10-20 beats at the wrist. She was treated by the technique described above. Operation entailed the removal of a large adherent malignant ovarian mass involving the sigmoid colon, which was resected, and an anastomosis was performed, with a colostomy above. During the operation, which took three hours, she received 400 ml. of blood to replace the estimated loss. Her pulse rate remained irregular throughout at 90-100 a minute. Her rectal temperature was 96° F. (35.6° C.) at the conclusion of the operation. She was rousable within three hours of the end of the operation and regained consciousness after six hours. Her rectal temperature rose to 100.2° F. (37.9° C.) during this period and her pulse rate remained irregular at the same rate. She has made an uneventful recovery.

Case 23.—A man aged 46, weighing 8 st. 6 lb. (53.5 kg.), had generalized Paget's disease with involvement of the spine. He had had spastic paraplegia and loss of sphincter control for eight months. A myelogram showed a spinal block at the level of the fourth dorsal vertebra. We obtained an autonomic blockade by the method described, and an extensive decompression of the spinal cord was undertaken by performing a bilateral laminectomy from the fourth to the eleventh dorsal vertebra. Blood loss was very rapid and was replaced by a transfusion of 4 pints (2.3 litres). His pulse remained steady at 90-100 a minute and his systolic pressure was sustained at just over 100 mm. Hg. Recovery was uneventful and his neurological condition was improving.

# Conclusions

It is impossible to assess statistically the advantages of any anaesthetic technique. From the small series of 36 cases involving really major surgery we have been impressed by the excellent condition of the patients, however extensive or long-continued the operation. We have had no deaths due either to the use of the method or to the operations performed. At no time during any of the procedures or during the post-operative period has the condition of the patient caused any anxiety. Furthermore, there has been no post-operative vomiting, nausea, or headache. The patients require less nursing care than normal, heavy post-operative sedation is not required, and there have been none of the post-operative complications which might have been expected to follow such major surgery. The patients are contented with this technique, for, although they can be roused,

most of them have complete amnesia from the time they leave the ward until six to eight hours after the operation. The freedom from post-operative pain and restlessness during this period seems to aid their recovery, for when the autonomic blockade has worn off they are cheerful, rested, and relatively free from pain.

The great advantage of this modification of Laborit's technique has been that we are now able confidently to undertake the anaesthetic care of patients who previously would have caused great anxiety, or would have been considered unfit to withstand major surgical intervention.

#### Summary

A brief account is given of a simplified method of producing autonomic blockade, as a method of preventing surgical shock during and immediately after major operations. The patient's condition has been better, both during and after the operation, than when conventional anaesthetic techniques have been used.

We would like to thank our colleagues and the nursing staff of the hospitals at which this work has been done for their sustained interest, and also Messrs. May & Baker Ltd. for supplying the drugs used.

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# THE BACTERIAL CONTENT OF HUMAN SMALL INTESTINE IN DISEASE OF THE STOMACH

BY

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It has already been shown (Cregan and Hayward, 1953) that when the human intestinal tract is healthy the small intestine is not colonized by a resident flora. Such organisms as are found there are so few in number that they must be regarded as transient contaminants passing through with the ingesta. The present work was undertaken to determine the effect of disease of the stomach on the flora of the small intestine. The results showed that neither a low gastric acidity nor the presence of a profuse flora in the stomach necessarily lead to the development of a resident flora in the small intestine. The antibacterial mechanism operating in the small intestine is therefore independent of the gastric germicidal barrier.

# Experimental

The patients chosen for the experiment were undergoing operation for gastric or duodenal ulcers or gastric carcinoma. In addition, there was one patient with a subtotal gastrectomy of two years' standing and a small oesophageal hiatal hernia. He was operated on for recurring haematemesis and melaena. All had been given light nourishment and had then fasted for at least four hours before the operation.

The methods of collection and bacteriological examination of specimens and evaluation of results were exactly as previously described (Cregan and Hayward, 1953), and are stated only briefly here. The contents of the intestine were removed directly through the bowel wall with syringes. Thus the possibility of contamination was reduced to a minimum, the levels of the intestine sampled could be anatomically defined, and parts of the intestine remote from the diseased stomach but exposed during the operation could be sampled. A standard bacteriological procedure was followed with all specimens so that results could be assessed quantitatively as well as qualitatively, the degree of growth being graded from  $\pm$  to +++. It was shown (Cregan and Hayward, 1953) that + or  $\pm$  growth indicated a transient flora and that ++ or +++ growth indicated a resident flora at the site sampled.

#### Results

Twenty-two cases were included in the investigation, and in each case the sites sampled were the upper jejunum, the mid-gut, and the lower ileum within 8 to 12 in. (20 to 30 cm.) of the ileo-caecal sphincter. In addition the stomach was sampled in all but four cases. The quantitative results are shown in Table I and the qualitative results in Table II.

#### Effect of Gastric Acidity and of Profuse Contamination of the Stomach

Of the 14 cases in which gastric acidity was determined, seven showed normal acidity or hyperacidity. The stomach, the upper jejunum, and the mid-gut were either sterile or contained only a transient flora in all of these seven cases. The lower ileum was colonized by a resident flora in three of them. These findings do not differ significantly from those in normal subjects. The remaining seven cases in which gastric acidity was determined showed hypoacidity or achlorhydria. In four of these (Cases 8, 9, 10, and 11) the flora of the small intestine did not differ from normal, and in the other three both the stomach and the upper jejunum contained a resident flora, but by the time the intestinal contents had reached the mid-gut their bacterial content had been reduced to a transient flora. It is apparent that the subnormal gastric acidity of this group of cases did not affect the normal ability of the small intestine to prevent multiplication of bacteria in its lumen and to destroy large numbers of bacteria entering it from a heavily contaminated stomach.

Of the eight cases in which gastric acidity was not tested, six were of advanced gastric carcinoma and almost certainly had a low gastric acidity. The results from this group confirm the finding that when large numbers of bacteria enter a normal small intestine from a diseased stomach they are destroyed by the time the mid-gut is reached, if not earlier. In only two of the seven cases in which the stomach contained a resident flora (Nos. 17 and 21) did the profuse contamination persist even as far as the upper jejunum.

Cases 9 and 10, with only a transient flora in the stomach, indicate that lowered gastric acidity, even achlorhydria, is not necessarily accompanied by an increase of bacteria in the stomach.

#### **Qualitative Results**

The qualitative results are shown in Table II. As in the study of cases in which the intestinal tract was normal, the organisms found in the upper intestine in the present investigation were predominantly Gram-positive species of the general type more commonly associated with the mouth than with the lower intestinal tract. However, Gram-negative species of faecal type were found more often in this study, and in Table I a resident flora is designated oral or faecal in type. It must be noted that this designation is not intended to suggest the origin of the organisms.

In any one patient there was a correlation between the species found at each level of the tract. There was no apparent association between particular species and the disease or the general condition of the patient. In particular, Candida albicans, which has been said to be commonly associated with carcinoma of the stomach, and the toxin-

TABLE I.—Quantitative Results

Case No.	Gastric Acidity	Date	Disease	Operation	Stomach	Upper Jejunum	Mid-gut	Lower Ileum
1	Hyperacidity	13/7/51	Carcinoma of lower oesophagus	Partial oesophagectomy. Total	-	-		
$\frac{2}{3}$	,,	6/7/51 2/10/52	invading stomach Duodenal ulcer	gastrectomy Subtotal gastrectomy. Billroth I Subtotal gastrectomy	± -	<u>+</u>	±	+ (F)
<b>4</b> 5	Normal "	17/4/52 13/5/52	Duodenal ulcer. Pyloric stenosis Duodenal ulcer. Small perforation and perigastric abscess	" " " "	N.T. ±	_	土	+ (F)
6 7	,,	12/9/51 11/7/52	Laparotomy Gastric ulcer	Gastrotomy. Biopsy of stomach Subtotal gastrectomy	N.T. ±	± -	± -	+ (F) ±
8 9	Hypoacidity	13/4/51 22/6/51	Gastric ulcer Large high gastric ulcer	Subtotal gastrectomy Total gastrectomy	N.T.	±	-	+ <b>(F)</b>
10	Achlorhydria	10/6/52	Huge gastric ulcer penetrating	Subtotal gastrectomy	土土	±	±	_
11	,,	4/5/51	liver and pancreas Extensive carcinoma of cardia and upper end of stomach	Total gastrectomy	N.T.	±	土	土
12	,,	13/2/52	Advanced carcinoma of cardia of stomach; peritoneal deposits	Abdomino-thoracic exploration. Souttar's intubation	+ <b>(O)</b>	+ (O)	±	±
13	,,	30/4/52	Carcinoma of gastric fundus invad-	Laparotomy	+ (F)	+ (F)	土	+ (F)
14	,,	9,7'52	ing pancreas and diaphragm Haematemesis and melaena follow- ing subtotal gastrectomy for ulcer two years prevously. Oesophageal hiatal hernia	Total gastrectomy. Repair of diaphragm	+ (F)	+ (F)	±	+ (F)
15	Gastric acidity	24/10/51	Advanced carcinoma of stomach	Laparotomy	+ (O)	±	_	+ (F)
16	not tested	10/10/51	with peritoneal spread Advanced carcinoma of upper stomach. Peritoneal invasion.	Oesophago-jejunal anastomosis (short-circuit)	+ (O)	±	±	+ (F)
17	,, ,,	24/7/51	Liver metastases Advanced gastric carcinoma. Peritoneal spread and metastases	Laparotomy	+ (O+F)	+ (O+F)	±	+ (O+F)
18	,, ,,	18/5/51	Gastric carcinoma. Pyloric ob-	Subtotal gastrectomy	+ <b>(O</b> )	土	±	N.T.
19	,, ,,	29/8/51	Carcinoma of cardia and upper	Left thoraco-abdominal. Total gastrectomy. Splenectomy	-	-	-	+ (O)
20	,, ,,	2/7/52	Extensive gastric carcinoma invad-	Total gastrectomy. Partial	+ (O)	±	土	±
21 22	" "	20/3/51 2/10/52	ing oesophagus Double gastric ulcer. Gastritis Gastric ulcer	oesophagectomy. Splenectomy Subtotal gastrectomy	+ (O) + (O)	+ (O)	±	+ (F) + (O)

BRITISH MEDICAL JOURNAL

formers, Cl. welchii, Str. pyogenes, and Staph aureus, were closely watched, but their presence had no apparent significance.

TABLE II.—Qualitative Results

	1		1
Site of Sampling	No. of Subjects	Gram-positive Species	Gram-negative Species
Stomach	18	Str. mitis (16)  " acidominimus (1) " MG (2) " uberis (2) " salivarius (1) " sp., variety 2 (1) " pyogenes (1) β-haemolytic streptococus, not Groups A, B, B, or G (2) Str. liquefaciens (1) Staph. aureus (2) " lactis (3) " saprophyticus (1) Lactobacillus sp. (1) Bacillus sp. (1) Cl. welchii (4) Candida albicans (4) " krusei (3) Monilia parapsilosis (2)	Bact. coli, type I (5) ", Intermediate, type I (2) Bact. aerogenes, type I (1 "Paracolon" sp. (1) Pseudomonas sp. (1) H. influenzae (1)
Upper jejunum	22	Str. mitis (19)  " MG (4)  " uberis (1)  " salivarius (2)  " s.b.c. (1)  " sp., variety 2 (1)  β-haemolytic strepto- coccus, not Groups A,  B, C, or G (1)  Staph. aureus (2)  " lactis (5)  " saprophyticus (2)  Lactobacillus sp. (4)  Bacillus sp. (1)  Cl. welchii (3)  Candida albicans (3)  " krusei (3)  Monilia parapsilosis (2)	Bact. coli, type I (5) ", Intermediate, type I (1) Bact. aerogenes, type I (2) ", II (2) Paracolon sp. (1) Pseudomonas sp. (1) Veillonella gazogenes (1)
Mid-gut	22	Str. mitis (13)  " MG (5) " acidominimus (1) " salivarius (2) " sp., variety 2 (1) " faecalis (1) " durans (1) Staph. aureus (1) " lactis (3) " saprophyticus (1) Lactobacillus sp. (1) Bacillus sp. (1) Bacillus sp. (1) Cl. welchii (3) " multifermentans (1) " butyricum (1) Candida abicans (1) Monilia parapsilosis (1)	Bact. coli type I (4) " " Intermediate, type I (1) Bact. aerogenes, type I (1) Pseudomonas sp. (1)
Lower ileum	21	Str. mitis (8)  " MG (3)  " salivarius (5)  " sp., variety 2 (1)  " sb.e. (4)  " pyogenes (1)  β-haemolytic streptococcus, not Groups A,  B, C, or G (2)  Str. faecalis (2)  " liquefaciens (1)  Staph. aureus (2)  " lactis (2)  " lactis (2)  " saprophyticus (2)  " afermentans (1)  Lactobacillus sp. (3)  Cl. welchii (6)  Corynebacterium sp. (2)  Candida albicans (1)  " krusei (1)  Monilia parapsilosis (1)	Bact. coli, type I (8) " Intermediate, type I (5) Bact. coli, Intermediate, type II (1) Bact. aerogenes, type I (5) " II (1) Paracolon sp. (7) Pseudomonas sp. (2) H. para-influenzae (1) Achromobacter sp. (1)

#### Discussion

In all these 22 patients undergoing gastric operations the mid-gut (lower jejunum or upper ileum) yielded at most a transient flora, although in 10 of the cases the gastric germicidal barrier was defective and the stomach was heavily contaminated. Even in the case of subtotal gastrectomy of two years' standing in which there had been prolonged reduction of stomach secretions the mid-gut yielded only a transient flora (actually  $\pm$  growth). The other cases show that advanced disease of the stomach, with associated physiological and anatomical changes, does not encourage the development of a resident bacterial flora in the small

Therefore an antibacterial mechanism, distinct from that of the stomach, must operate in the small intestine. Failure to recognize that there are two independent mechanisms and that the stomach mechanism may be defective and the small intestine mechanisms be intact has led to the widely held misconception that if the gastric secretions are reduced or absent organisms from the large bowel will invade the small intestine. For example, Wells and Welbourn (1951) state that achlorhydria following gastrectomy causes "bacteria which normally inhabit the colon to grow freely all the way up the small intestine and in the gastric stump." This view has arisen from studies of samples, generally only from the duodenum and the stomach, removed by passing a tube via the mouth (Knott, 1927: Ricen, Sears, and Downing, 1928; Torrey, Kahn, and Salinger, 1930; Dick, 1941, quoted by Bethell et al., 1942; French and Thompson, quoted by Frazer, 1949).

The results reported here show that a consideration of a single specimen from the upper small intestine could be misleading. The upper jejunum was heavily contaminated in 5 out of 10 cases in which the stomach contained a resident flora (Table I), but the scarcity of organisms further on in the mid-gut in all cases showed that this was not due to an invasion from the large intestine but to an abnormally heavy intake of organisms from the diseased stomach. In all cases reported here the antibacterial mechanism of the small intestine was functioning, whether gastric acidity was increased, decreased, or normal.

Further, this misconception has led to the suggestion that vitamin-B deficiencies in the post-gastrectomy syndrome (Welbourn, Hughes, and Wells, 1951; Wells and Welbourn. 1951), in the sprue syndrome, and possibly also in pernicious anaemia, pellagra, and nutritional megalocytic anaemia (Frazer, 1949) arise because bacteria invading the small intestine deprive the host of vitamins. This suggestion cannot rest on the fact that the stomach secretions are deficient. Until it has been shown that the small intestine's antibacterial mechanism is defective in these cases the theory has no sound foundation.

The work of Sinek and Reimann (1931) supports the findings reported here. They found that low gastric acidity was not necessarily associated with an increase in the incidence of *Bact. coli* in the duodenum.

More recently Barber and Franklin (1946), who examined swabs taken from the stomach and duodenum during stomach operations, found that, although the stomach was infected in 25 out of the 50 cases they examined, the duodenum was infected in only seven. They do not draw special attention to this fact, and the misconception has persisted in spite of their work.

No indication of the factors that determine whether a resident flora is established in the lower ileum can be seen from this work. Whereas 12 out of 21 cases yielded a profuse ileal flora in these cases of disease of the stomach, only 2 out of 14 did so when the intestinal tract was normal (Cregan and Hayward, 1953).

# Summary

In cases of disease of the stomach presenting for operation the small intestine was found to contain only a sparse transient population, irrespective both of gastric acidity and of the degree of contamination of the stomach.

It is deduced that the small intestine has an antibacterial mechanism which is independent of the gastric germicidal barrier.

We would like to thank Professor S. D. Rubbo, professor of bacteriology, University of Melbourne, for his constant helpful advice; Mr. E. S. R. Hughes, acting out-patient surgeon, Royal Melbourne Hospital, for providing the specimens of two of the cases; Dr. Jacqueline Walker for assistance with the identification of species of Candida; the staff of the Royal Melbourne Hospital; and Miss Marjorie Krohn for technical assistance. One of us (J. C.) was in receipt of a personal grant from the National Health and Medical Research Council.

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# TREATMENT OF ACUTE PANCREATITIS WITH HEXAMETHONIUM BROMIDE

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In 1889 Fitz described three types of acute pancreatitis haemorrhagic, gangrenous, and suppurative—based on the gross pathology of the gland. McWhorter (1932) collected 64 cases and classified them as follows: (1) acute or subacute pancreatitis in which there was no haemorrhage but in which the gland was enlarged, oedematous, and very hard; (2) the haemorrhagic, in which haemorrhages were present but there was no evidence of gangrene or suppuration; (3) cases with gross necrosis or gangrene but no suppuration; and (4) cases with suppuration or definite abscess formation.

A classification on an aetiological basis suggested by McWhorter (1932) and Jones (1943) adds little to our knowledge.

A. Infectious Origin.—(1) By extension along the lymphatics; (2) by extension from the blood stream; (3) by extension along the pancreatic ducts, from the duodenum or from the bile ducts; (4) by direct extension from infected foci; (5) following activation of bacteria in the normal gland; (6) by bacterial permeability from adjacent diseased

B. Non-infectious Origin.—(1) Mechanical, including stasis in the ducts. (2) Chemical, and originating in activated ferments resulting from (a) bile; (b) duodenal contents; (c) degenerated duct contents; (d) autolysis. (3) Degenerative changes in the pancreas: (a) secondary to benign or malignant tumours; (b) resulting from vascular degeneration or haemorrhage; (c) toxic changes following systemic disease. (4) Trauma.

C. A Combination of Two or More of the Above Factors.

The disease most commonly occurs in the fifth and sixth decades in obese males. Bisgard and Baker (1940) pointed out the frequent association of cholelithiasis. The disease may affect the whole gland or may be limited to the head, the body, or the tail. The extent of necrosis depends upon the violence of the biochemical explosion. If small areas alone are involved they may be absorbed or converted into fibrous tissue; but, if large, the necrotic areas soon slough or suppurate.

Ian Aird (1949) states that "a complicated network of theory has been woven around pancreatitis in order to relate it to gall-bladder disease but without any conclusive or all-embracing theory." We believe that pancreatitis is due to a vascular accident and that the findings of biliary pathology are coincidental.

One of us was impressed with the similarity in pathology of thrombosis and embolism in other organs, and treated with systemic heparin two cases of acute pancreatitis confirmed by exploratory laparotomy. The results were satisfactory, but led to a continuous ooze of blood from the suture line in each case. Although pain was relieved the loss of blood from the suture lines was sufficient to require intravenous blood transfusion. We concluded that the systemic heparin may have been responsible for the recovery of these two cases, which we classified, according to McWhorter's criteria. as gangrenous lesions of part of the head.

The following two cases were treated with hexamethonium drugs, and had a very smooth convalescence.

#### Case 1

An obese male aged 64 had been in good health until the morning of May 5, 1952, when he was seized with a sudden agonizing abdominal pain. It was located around the umbilicus and the left flank.

On examination he was found to be very shocked, and was frequently vomiting small amounts of bile-stained fluid. His face was livid and beaded with sweat, and the extremities were cold and damp. The abdomen was uniformly rigid, with maximum tenderness around the umbilicus. No other abnormal physical signs were discovered. A provisional diagnosis of pancreatitis was made. This was confirmed by exploratory laparotomy. The relevant findings were an injected peritoneum and a hard oedematous dusky-red pancreas with darker patches in the head. The proximal 3-4 in. (7.5-10 cm.) of the small gut was distended and scattered and traced with lymphatic vessels. The omentum revealed fat necrosis. The biliary tract was normal on palpation. The abdomen was closed without drainage.

The day following exploratory laparotomy the patient remained in great pain, and for this reason a bilateral posterior splanchnic block was performed with 1/2,000 amethocaine. The relief from pain was dramatic and the improvement in the clinical condition most marked. Pain began to return after complete control for approximately six hours. It seemed reasonable to believe that ganglion-blocking agents, such as hexamethonium, would similarly relieve pain, and that administration of this drug would have none of the difficulties or dangers of repeated splanchnic blocks. Oral hexamethonium bromide, 250 mg., was given via the indwelling Ryle's tube twice a day, and the activity of the drug was observed by blood-presssure readings, carried out by the nursing staff. Pain disappeared after six hours, and the next day it was possible to assess the patient as convalescent. Treatment with hexamethonium was continued for five days, the patient being discharged, cured, on the tenth day. He remained well up to the time of submitting this report.

#### Case 2

This patient was a man aged 52. His history was complicated by a previous perforation of a peptic ulcer six years previously. Three years before his present illness he was subjected to gastrectomy, this being followed by a complete remission of his indigestion.

On the day of admission (August 9, 1952) he was seized with violent upper abdominal pain, mainly localized to the right hypochondrium. He frequently vomited small amounts with each severe attack of pain, which appeared to be colicky in type. The abdomen was explored and a considerable quantity of free sero-sanguineous fluid was found. The great omentum was studded with islets of fat necrosis and several feet of the small intestine was injected, distended, and traced with lymphatic vessels. The pancreas was hard, oedematous, and of a deep-red colour over the whole visible surface of the gland. The biliary tract felt normal on palpation. The abdomen was closed without drainage.

Hexamethonium, 250 mg., was given as soon as the patient was conscious, and this was continued twice a day for the next seven days, four-hourly blood-pressure readings